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ENTECH file  
NEWS 5 May 17 CAOLD now has searchable data back to 1907  
  
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DICTIONARY FILE UPDATES: 21 MAY 99 HIGHEST RN 223568-03-4

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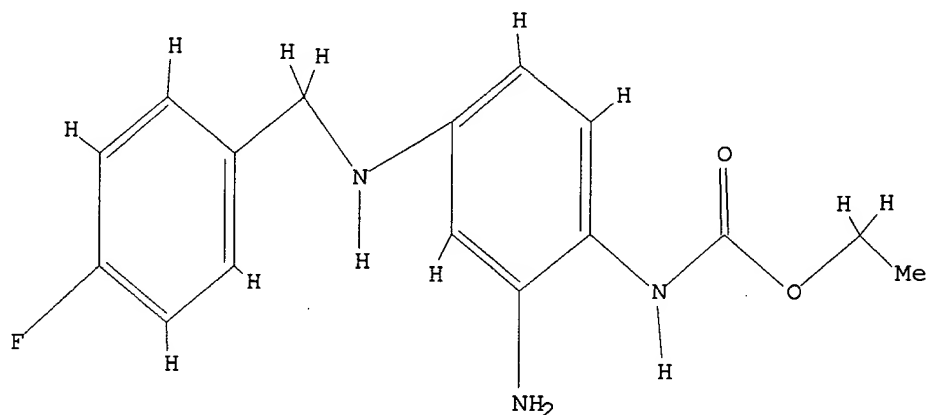
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L1        STRUCTURE UPLOADED

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L1                STR



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SAMPLE SEARCH INITIATED 11:27:13 FILE 'REGISTRY'  
SAMPLE SCREEN SEARCH COMPLETED -        0 TO ITERATE  
100.0% PROCESSED        0 ITERATIONS        0 ANSWERS  
SEARCH TIME: 00.00.01

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                              BATCH    \*\*COMPLETE\*\*  
PROJECTED ITERATIONS:        0 TO        0  
PROJECTED ANSWERS:            0 TO        0

L2                0 SEA SSS SAM L1

=> s l1 full

FULL SEARCH INITIATED 11:27:19 FILE 'REGISTRY'  
FULL SCREEN SEARCH COMPLETED -        58 TO ITERATE  
100.0% PROCESSED        58 ITERATIONS        2 ANSWERS  
SEARCH TIME: 00.00.01

L3                2 SEA SSS FUL L1

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FULL ESTIMATED COST	120.30	120.45

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FILE COVERS 1967 - 24 May 1999 VOL 130 ISS 22  
FILE LAST UPDATED: 24 May 1999 (19990524/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

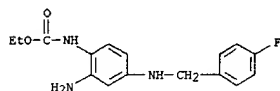
This file supports REGISTRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

=> s 13

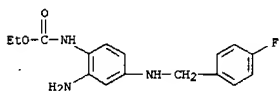
L4                    12 L3

=> d l4 1-12 abs ibib hitstr

L4 ANSWER 1 OF 12 CAPLUS COPYRIGHT 1999 ACS  
 AB The structure of the anticonvulsant substance N-[2-amino-4-(4-fluorobenzylamino)-phenyl]ethylcarbamate (INN: retigabine) was proved by IR, UV, <sup>1</sup>H NMR, <sup>13</sup>C NMR and mass spectra. Retigabine is practically insol. in a neutral aq. medium at 20 .degree. (S .apprx. 0.07 g/l). The soly. of the substance in 0.1 N HCl is about 16 g/l. In DMF, retigabine is freely sol. (S .apprx. 186 g/l). The pK-value is about 3.7. The partition coeff. P = Octanol/CWater at 37 .degree. ranging from 0.4 at pH .apprx. 1 to about 150 at pH .gt;oreq. 5.  
 ACCESSION NUMBER: 1998:807142 CAPLUS  
 DOCUMENT NUMBER: 130:57310  
 TITLE: Structure and physicochemical properties of N-[2-amino-4-(4-fluorobenzylamino)-phenyl]ethylcarbamate, retigabine Thiel, W.  
 AUTHOR(S):  
 CORPORATE SOURCE: Arzneimittelwerk Dresden G.m.b.H., Radebeul, D-01445,  
 SOURCE: Germany Pharmazie (1998), 53(12), 865-869  
 CODEN: PHARAT; ISSN: 0031-7144  
 PUBLISHER: Govi-Verlag Pharmazeutischer Verlag  
 DOCUMENT TYPE: Journal  
 LANGUAGE: German  
 IT 150812-12-7, Retigabine  
 RL: ANT (Analyte); PRP (Properties); ANST (Analytical study) (structure and physicochem. properties of N-[2-amino-4-(4-fluorobenzylamino)-phenyl]ethylcarbamate, retigabine)  
 RN 150812-12-7 CAPLUS  
 CN Carbamic acid, [2-amino-4-[[[(4-fluorophenyl)methyl]amino]phenyl]-, ethyl ester (9CI) (CA INDEX NAME)



L4 ANSWER 2 OF 12 CAPLUS COPYRIGHT 1999 ACS (Continued)  
 Department of Neurophysiology, Humboldt University  
 Germany  
 SOURCE: Berlin, Tucholskystrasse 2, Berlin, D-10117, Naunyn-Schmiedeberg's Arch. Pharmacol. (1999), 33-39  
 CODEN: NSAPCC; ISSN: 0028-1298  
 PUBLISHER: Springer-Verlag  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 IT 150812-12-7, Retigabine  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (retigabine effect on different patterns of 4AP-induced epileptiform activity in rat entorhinal cortex hippocampal slices)  
 RN 150812-12-7 CAPLUS  
 CN Carbamic acid, [2-amino-4-[[[(4-fluorophenyl)methyl]amino]phenyl]-, ethyl ester (9CI) (CA INDEX NAME)

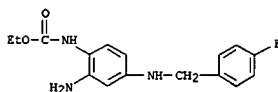


L4 ANSWER 2 OF 12 CAPLUS COPYRIGHT 1999 ACS  
 AB The purpose of this study was to evaluate the effects of the new anticonvulsant drug N-(2-amino-4-[fluorobenzylamino]-phenyl) carbamic acid Et ester (retigabine, D-23129, ASTA Medica, Dresden, Germany) on different patterns of epileptiform activity induced by 4-aminopyridine (4AP) in rat entorhinal cortex hippocampal slices. Application of 4AP (100 mM) induced in entorhinal cortex two different types of epileptiform activities: seizure-like events (SLE) and interictal epileptiform discharges (IED). Bicuculline (10 mM) changed 4AP-induced SLE and IED to recurrent epileptiform discharges (RED). IED were isolated after blockade of the SLE by glutamate receptor antagonists for .alpha.-amino-3-hydroxy-5-methylisoxazole-4-propionic acid (AMPA) and N-methyl-D-aspartate (NMDA) receptors, i.e. 1,2,3,4-tetrahydro-6-nitro-2,3-dioxo-benzo[f]quinoxaline-7-sulfonamide (NBQX, 10 mM) and 2-amino-5-phosphonovaleric acid (APV, 30 mM). Anticonvulsant properties of retigabine were evaluated as effect on the frequency and amplitude of SLE, IED and RED. Retigabine suppressed all types of epileptiform events in a dose dependent and reversible manner. SLE were suppressed in 71.4 and 100% of slices by 5 and 10 mM, resp. The frequency of IED was significantly reduced by 20 mM retigabine (40.9+-24.5%) and IED were blocked completely by 50 mM retigabine. When IED were isolated by application of glutamate antagonists 20 mM retigabine was sufficient to block this activity completely. RED induced by combined application of bicuculline and 4AP were blocked in 71.4% of the tested slices with 100 mM retigabine. The frequency of the RED in the remaining slices was reduced by 96.1+-6.1%. We conclude that retigabine acts on a large variety of different epileptiform activities in temporal lobe structures that are known to develop readily pharmacoresistant seizures.  
 ACCESSION NUMBER: 1998:792703 CAPLUS  
 DOCUMENT NUMBER: 130:261905  
 TITLE: Effects of retigabine (D-23129) on different patterns of epileptiform activity induced by 4-aminopyridine in rat entorhinal cortex hippocampal slices  
 AUTHOR(S): Armand, V.; Rundfeldt, C.; Heinemann, U.  
 CORPORATE SOURCE: Universitatklinikum Charite, Institute of Physiology,

L4 ANSWER 3 OF 12 CAPLUS COPYRIGHT 1999 ACS  
 AB Novel derivs. of 2-amino-4-(4-fluorobenzylamino)-1-ethoxycarbonyl-aminobenzene (I) that may be of pharmaceutical use (no data) are prep'd. by recrystn. of I from non-polar, polar or dipolar aprotic solvents. The new forms are defined by X-ray diffraction patterns, IR spectra, and differential scanning calorimetry.  
 ACCESSION NUMBER: 1998:490710 CAPLUS  
 DOCUMENT NUMBER: 129:104236  
 TITLE: Derivatives of 2-amino-4-(4-fluorobenzylamino)-1-ethoxycarbonyl-aminobenzene for pharmaceutical use and their preparation  
 INVENTOR(S): Meisel, Peter; Landgraf, Karl-Friedrich; Schaefer, Juergen; Thiel, Wilfried; Rischer, Matthias; Olbrich, Alfred; Kutscher, Bernhard  
 PATENT ASSIGNEE(S): Asta Medica A.-G., Germany  
 SOURCE: Ger. Offen., 10 pp.  
 CODEN: GWXXEX  
 DOCUMENT TYPE: Patent  
 LANGUAGE: German  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

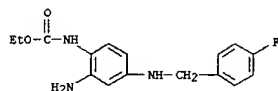
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19701694	A1	19980723	DE 97-19701694	19970120
WO 9831663	A1	19980723	WO 98-EP86	19980109
W: AU, BG, BR, CA, CN, CZ, HU, ID, IL, IS, JP, KR, MX, NO, NZ, PL, RO, RU, SK, TR, UA				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9862081	A1	19980807	AU 98-62081	19980109
PRIORITY APPLN. INFO.:			DE 97-19701694	19970120
			WO 98-EP86	19980109

IT 150812-12-7D, derivs.  
 RL: RCT (Reactant)  
 (derivs. of 2-amino-4-(4-fluorobenzylamino)-1-ethoxycarbonyl-aminobenzene for pharmaceutical use and their prepn.)  
 RN 150812-12-7 CAPLUS  
 CN Carbamic acid, [2-amino-4-[[[(4-fluorophenyl)methyl]amino]phenyl]-, ethyl ester (9CI) (CA INDEX NAME)



AB The patch-clamp technique was used to measure currents passing through K<sup>+</sup> channels in neuronal cell preps. Retigabine (D-23129, N-(2-amino-4-((4-fluorobenzylamino)-phenyl) carbamic acid Et ester) activated a K<sup>+</sup> conductance in slightly depolarized NG108-15 neuronal cells in a dose-dependent manner (0.1-10 .mu.M). At the K<sup>+</sup> reversal potential, no current could be elicited and in hyperpolarized cells the current was reversed. A similar current was elicited in primary cultures of mouse cortical neurons and in differentiated hNT cells, a cell line derived from human neuronal cells. At higher concns., retigabine also partially blocked voltage activated K<sup>+</sup> currents. None of the tested anticonvulsants, phenytoin, carbamazepine and valproate and none of the K<sup>+</sup> channel openers cromakalim, diazoxide and pinacidil exerted a similar effect. The current was not affected by the K<sup>+</sup> channel blocker glibenclamide (10 .mu.M) but was fully blocked by application of Ba<sup>2+</sup> (10.8 mM). Exchange of K<sup>+</sup> with cesium in the intracellular space also fully abolished the current. It can be expected that the K<sup>+</sup> channel opening effect contributes to the anticonvulsant activity of retigabine.

ACCESSION NUMBER: 1997:646571 CAPLUS  
DOCUMENT NUMBER: 127:326363  
TITLE: The new anticonvulsant retigabine (D-23129) acts as an opener of K<sup>+</sup> channels in neuronal cells  
AUTHOR(S): Rundfeldt, Chris  
CORPORATE SOURCE: Department of Pharmacology, Arzneimittelwerk Dresden  
Meissner GmbH, Corporate R and D, ASTA Medica Group, Strasse 35, Radebeul, D-01445, Germany  
SOURCE: Eur. J. Pharmacol. (1997), 336(2/3), 243-249  
CODEN: EUPHAZ; ISSN: 0014-2999  
PUBLISHER: Elsevier  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
IT 150812-12-7, D-23129  
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(new anticonvulsant retigabine (D-23129) acts as opener of K<sup>+</sup> channels in neuronal cells)  
RN 150812-12-7 CAPLUS  
CN Carbamic acid, [2-amino-4-[[[(4-fluorophenyl)methyl]amino]phenyl]-, ethyl ester (9CI) (CA INDEX NAME)



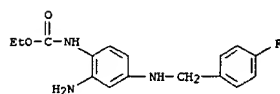
AB The title compd. (I) and its salts are useful as neuroprotectants for prevention and treatment of stroke, impaired cerebral circulation, and neurodegenerative diseases. Thus, a learning deficit in rats with a ligated carotid artery was reversed by administration of I (2 mg/kg i.p.).

ACCESSION NUMBER: 1997:377765 CAPLUS  
DOCUMENT NUMBER: 126:338857  
TITLE: Use of 4-amino-4-(4-fluorobenzylamino)-1-ethoxycarbonylaminobenzene for prevention and treatment of sequelae of poor cerebral circulation or neurodegenerative diseases  
INVENTOR(S): Rostock, Angelika; Tober, Christine; Rundfeldt, Chris  
PATENT ASSIGNEE(S): Bartsch, Reni  
SOURCE: Asta Medica Ag, Germany  
Ger. Offen., 5 pp.  
CODEN: GWXXEX  
DOCUMENT TYPE: Patent  
LANGUAGE: German  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

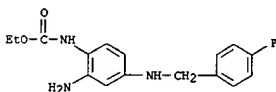
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19539861	A1	19970430	DE 95-19539861	19951026
WO 9715300	A2	19970501	WO 96-DE1951	19961015
WO 9715300	A3	19970703		
W: AU, BR, BY, CA, CZ, HU, IL, JP, KR, MX, NO, NZ, PL, RU, SK, UA RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9715400	A1	19970515	AU 97-15400	19961015
EP 857065	A2	19980812	EP 96-945354	19961015
EP 857065	B1	19990407		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, IE, FI				
AT 178487	E	19990415	AT 96-945354	19961015
CA 2188841	AA	19970427	CA 96-2188841	19961025
US 5852053	A	19981222	US 96-736166	19961028
US 5849789	A	19981215	US 97-937420	19970925
NO 9801503	A	19980402	NO 98-1503	19980402
PRIORITY APPLN. INFO.: DE 95-19539861 19951026 WO 96-DE1951 19961015 US 96-736166 19961028				

IT 150812-12-7  
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(use of amino(4-fluorobenzylamino)ethoxycarbonylaminobenzene for prevention and treatment of poor cerebral circulation or neurodegenerative diseases)  
RN 150812-12-7 CAPLUS  
CN Carbamic acid, [2-amino-4-[[[(4-fluorophenyl)methyl]amino]phenyl]-, ethyl

L4 ANSWER 5 OF 12 CAPLUS COPYRIGHT 1999 ACS (Continued)  
ester (9CI) (CA INDEX NAME)

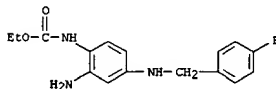


L4 ANSWER 6 OF 12 CAPLUS COPYRIGHT 1999 ACS  
AB The metabolic profile of D-23129, a new anticonvulsant agent, was studied in vitro using human liver microsomes and fresh liver slices. Oxidative metab. appeared to be minimal with D-23129. The percent mean total radioactivity not assocd. with the parent compd. recovered from oxidative metab. studies from three individual liver donors was 0.cntdot.78.+-.0.cntdot.6 SD and was not significantly different from [14C]-D-23129 incubated with heat inactivated microsomes, mean = 0.cntdot.58.+-.0.cntdot.4 SD. Phase II conjugation dominated the metab. of D-23129 producing two distinct N-glucuronides as the primary metabolites. These metabolites were identified by electrospray ionization LC/MS. The apparent Km for one of the glucuronide metabolites was detd. in human liver microsome preps. from two individual liver donors to be 131 and 264 .mu.M resp. Vmax detd. for the same microsomal preps. yielded 48.cntdot.9 and 59.cntdot.p pmol/min/mg protein. ACCESSION NUMBER: 1997:357310 CAPLUS DOCUMENT NUMBER: 127:75470 TITLE: In vitro glucuronidation of D-23129, a new anticonvulsant, by human liver microsomes and liver slices AUTHOR(S): McNeilly, P. J.; Torchin, C. D.; Anderson, L. W.; Kapetanovic, I. M.; Kupferberg, H. J.; Strong, J. M. CORPORATE SOURCE: Laboratory Clinical Pharmacology, Office Pharmaceutical Sciences, Center Drug Evaluation Research, US Food Drug Administration, Laurel, MD, 20708, USA SOURCE: Xenobiotica (1997), 27(5), 431-441 CODEN: XENOBH; ISSN: 0049-8254 PUBLISHER: Taylor & Francis DOCUMENT TYPE: Journal LANGUAGE: English IT 150812-12-7, D-23129 RL: BPR (Biological process); BIOL (Biological study); PROC (Process) (in vitro glucuronidation of D-23129 by human liver microsomes and liver slices) RN 150812-12-7 CAPLUS CN Carbamic acid, [2-amino-4-[[[4-fluorophenyl)methyl]amino]phenyl]-, ethyl ester (9CI) (CA INDEX NAME)



L4 ANSWER 6 OF 12 CAPLUS COPYRIGHT 1999 ACS (Continued)

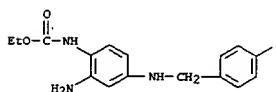
L4 ANSWER 7 OF 12 CAPLUS COPYRIGHT 1999 ACS  
AB A review, with 42 refs., of the chem., pharmacokinetics, and clin. pharmacol. of D-23129 as a new anticonvulsant. ACCESSION NUMBER: 1996:749838 CAPLUS DOCUMENT NUMBER: 126:26281 TITLE: D-23129: A new anticonvulsant compound AUTHOR(S): Kapetanovic, Izet M.; Rundfeldt, Chris CORPORATE SOURCE: National Institute Neurological Disorders and Stroke, National Institutes Health, Bethesda, MD, USA SOURCE: CNS Drug Rev. (1996), 2(3), 308-321 CODEN: CDREPB; ISSN: 1080-563X PUBLISHER: Nova Press DOCUMENT TYPE: Journal; General Review LANGUAGE: English IT 150812-12-7, D-23129 RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (D-23129: a new anticonvulsant compd.) RN 150812-12-7 CAPLUS CN Carbamic acid, [2-amino-4-[[[4-fluorophenyl)methyl]amino]phenyl]-, ethyl ester (9CI) (CA INDEX NAME)



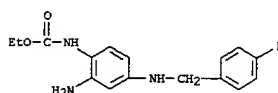
L4 ANSWER 8 OF 12 CAPLUS COPYRIGHT 1999 ACS  
 AB The anticonvulsant activity of the novel drug D-23129  
 (N-(2-amino-4-(4-fluorobenzylamino)phenyl)carbamic acid Et ester) was evaluated in  
 animal models of epileptic seizures. D-23129 was active after oral and i.p.  
 administration in rats and mice in a range of anticonvulsant tests at  
 nontoxic doses. The compd. was active against elec. induced seizures  
 (MES, ED50 rat p.o. = 2.87 mg/kg), against seizures induced chem. by  
 pentylenetetrazole (s.c. PTZ, ED50 mouse p.o. = 13.5 mg/kg),  
 picrotoxin and N-methyl-D-aspartate (NMDA) and in a genetic animal model, the  
 DBA/2 mouse. It was not active against seizures induced by bicuculline and  
 strychnine. Motor impairment, evaluated with the rotarod test and by  
 observation in the open field, was minimal at doses showing  
 anticonvulsant activity. D-23129 was very effective in elevating the threshold for  
 elec. and chem. induced seizures. Considering the dose increasing the MES  
 threshold by 50% (TID50 mouse i.p. = 1.6 mg/kg; TID50 rat i.p. = 0.72  
 mg/kg) and the TD50 obtained in the rotarod test, the protective  
 index of D-23129 is better than that of valproate and phenytoin. During 14  
 days chronic oral treatment with 15 mg/kg, no development of tolerance was  
 obsd. D-23129 thus presents an orally active, safe, broad spectrum  
 anticonvulsant agent, which is structurally unrelated to  
 anticonvulsants currently used. We expect that D-23129 will improve the treatment of  
 refractory seizures in humans.  
 ACCESSION NUMBER: 1996:374503 CAPLUS  
 DOCUMENT NUMBER: 125:104861  
 TITLE: D-23129: A new anticonvulsant with a broad  
 spectrum activity in animal models of epileptic seizures  
 AUTHOR(S): Rostock, Angelika; Tober, Christine; Rundfeldt,  
 Chris; Bartsch, Reni; Engel, Juergen; Polymeropoulos,  
 Emanuele E.; Kutscher, Bernhard; Loescher,  
 Wolfgang;  
 CORPORATE SOURCE: Hoenack, Dagmar; et al.  
 ASTA Medica Group, Department Pharmacology,  
 Radebeul, D-01445, Germany  
 SOURCE: Epilepsy Res. (1996), 23(3), 211-223  
 CODEN: EPIRES; ISSN: 0920-1211  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 IT 150812-12-7, D 23129  
 RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use);  
 BIOL (Biological study); USES (Uses)  
 D-23129 as new anticonvulsant with broad spectrum activity;  
 D-23129 as

L4 ANSWER 9 OF 12 CAPLUS COPYRIGHT 1999 ACS  
 AB The novel anticonvulsant drug D-23129  
 (N-(2-amino-4-(4-fluorobenzylamino)-  
 phenyl) carbamic acid Et ester) was evaluated in the amygdala  
 kindling model of complex partial seizures in rats. D-23129 exerts potent  
 anticonvulsant activity against both focal and generalized seizures  
 in animal models of epilepsy. After i.p. and oral administration in  
 kindled rats, the substance dose dependently increased the threshold for  
 induction of afterdischarges, exerting significant effects already after 0.01  
 mg/kg. In higher doses (2.5-5 mg/kg i.p., 10-15 mg/kg p.o.) D-23129 also  
 exerted anticonvulsant effects on other seizure parameters of  
 amygdala-kindled rats, i.e. seizure severity, seizure duration, total duration of  
 behavioral changes and afterdischarge duration. The adverse effects  
 of D-23129 were quantitated in the open field and in the rotarod test,  
 a std. test for motor impairment. D-23129 exerted no adverse effects on  
 behavior in doses up to 5 mg/kg i.p. and 15 mg/kg p.o. Comparing the adverse  
 effects between kindled and non-kindled rats, no differences were  
 found. The data demonstrate that D-23129 is more potent in the amygdala  
 kindling model of complex partial seizures than in other seizure models.  
 D-23129 is orally active and is devoid of neurotoxic effects in  
 anticonvulsant doses, thus indicating that this compd. has potential for  
 antiepileptic therapy.  
 ACCESSION NUMBER: 1996:347688 CAPLUS  
 DOCUMENT NUMBER: 125:76080  
 TITLE: D-23129: a potent anticonvulsant in the amygdala  
 kindling model of complex partial seizures  
 AUTHOR(S): Tober, Christine; Rostock, Angelika; Rundfeldt,  
 Chris; Bartsch, Reni  
 CORPORATE SOURCE: Department of Pharmacology, Corporate Research  
 and Development, ASTA Medica Group, Arzneimittelwerk  
 Dresden, Meissner Strasse 191, D-01445, Radebeul,  
 Germany  
 SOURCE: Eur. J. Pharmacol. (1996), 303(3), 163-169  
 CODEN: EJPHAZ; ISSN: 0014-2999  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 IT 150812-12-7, D 23129  
 RL: BAC (Biological activity or effector, except adverse); THU

L4 ANSWER 8 OF 12 CAPLUS COPYRIGHT 1999 ACS (Continued)  
 new anticonvulsant with broad spectrum activity)  
 RN 150812-12-7 CAPLUS  
 CN Carbamic acid, [2-amino-4-[[4-(4-fluorophenyl)methyl]amino]phenyl]-,  
 ethyl ester (9CI) (CA INDEX NAME)



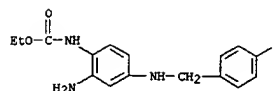
L4 ANSWER 9 OF 12 CAPLUS COPYRIGHT 1999 ACS (Continued)  
 (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (anticonvulsant effects of D-23129 in amygdala kindling model of  
 complex partial seizures)  
 RN 150812-12-7 CAPLUS  
 CN Carbamic acid, [2-amino-4-[[4-(4-fluorophenyl)methyl]amino]phenyl]-,  
 ethyl ester (9CI) (CA INDEX NAME)



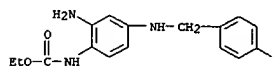
L4 ANSWER 10 OF 12 CAPLUS COPYRIGHT 1999 ACS  
 AB D-23129 [N-(2-amino-4-[(4-fluorobenzylamino)phenyl]carbamic acid Et ester] and D-20443 (dihydrochloride of D-23129) are promising anticonvulsant compds. with a broad spectrum activity in animal models of epilepsy. Their effects on de novo synthesis of excitatory (glutamate and aspartate) and inhibitory (GABA) amino acids were studied in rat hippocampal slices. Like phenytoin, carbamazepine, lamotrigine, losigamone, U54494A, and flupirtine, D-23129 and D-20443 were effective in preventing the effects of a chemoconvulsant, 4-aminopyridine, on de novo synthesis of the three amino acids. However, unlike the other compds., D-23129 and D-20443 also preferentially increased the concns. of newly synthesized GABA. Their effect on the neosynthesis of GABA was unique, dose dependent, and not tetrodotoxin sensitive. A total of 15 compds. (including std., new and candidate anticonvulsants) either had no effect on new GABA or decreased it. Therefore, D-23129 and D-20443 exhibited two different effects on de novo synthesis of neurotransmitter amino acids, both of which could potentially be anticonvulsant in nature.

ACCESSION NUMBER: 1996:93161 CAPLUS  
 DOCUMENT NUMBER: 124:194122  
 TITLE: The effects of D-23129, a new experimental anticonvulsant drug, on neurotransmitter amino acids in the rat hippocampus in vitro  
 AUTHOR(S): Kapetanovic, Izet M.; Yonekawa, Wayne D.; Kupferberg, Harvey J.  
 CORPORATE SOURCE: National Institute Neurological Disorders and Stroke, National Institutes Health, Bethesda, MD, 20892, USA  
 SOURCE: Epilepsy Res. (1995), 22(3), 167-73  
 CODEN: EPIRES; ISSN: 0920-1211  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 IT 150812-12-7 150812-13-8, D-20443  
 RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (effects of D-23129, a new exptl. anticonvulsant drug, on neurotransmitter amino acids in the rat hippocampus in vitro)  
 RN 150812-12-7 CAPLUS  
 CN Carbamic acid, [2-amino-4-[[[(4-fluorophenyl)methyl]amino]phenyl]-, ethyl ester (9CI) (CA INDEX NAME)

L4 ANSWER 10 OF 12 CAPLUS COPYRIGHT 1999 ACS (Continued)



RN 150812-13-8 CAPLUS  
 CN Carbamic acid, [2-amino-4-[[[(4-fluorophenyl)methyl]amino]phenyl]-, ethyl ester, dihydrochloride (9CI) (CA INDEX NAME)

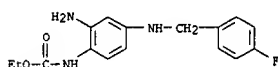


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L4 ANSWER 11 OF 12 CAPLUS COPYRIGHT 1999 ACS  
 AB D-20443 is an exptl. antiepileptic drug. Its mechanism of antiepileptic action is unknown. We evaluated the anticonvulsant effectiveness of D-20443 against sound-induced seizures in genetically epilepsy-prone rats (GEPRs). This compd. produced anticonvulsant effects against sound-induced seizures in moderate seizure GEPRs (GEPR-3s) at significantly lower doses than in severe seizure GEPRs (GEPR-9s). Based on these data and on the responses of GEPRs to other antiepileptic drugs, we predict that D-20443 will be a broad spectrum antiepileptic agent in humans. I.e., we predict that D-20443 will suppress both tonic/clonic and absence seizures in humans.

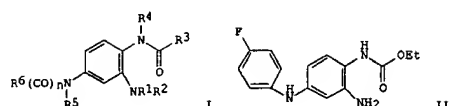
ACCESSION NUMBER: 1995:739590 CAPLUS  
 DOCUMENT NUMBER: 123:188283  
 TITLE: Anticonvulsant properties of D-20443 in genetically epilepsy-prone rats: prediction of clinical response  
 AUTHOR(S): Bailey, John W.; Cheong, Jae Hoon; Ko, Kwang Ho; Adams-Curtis, Leah E.; Jobe, Phillip C.  
 CORPORATE SOURCE: Department of Basic Sciences, University of Illinois College of Medicine at Peoria, P.O. Box 1649, Peoria, IL, 61656, USA  
 SOURCE: Neurosci. Lett. (1995), 195(2), 77-80  
 CODEN: NELED5; ISSN: 0304-3940  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 IT 150812-13-8, D 20443  
 RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (D-20443 anticonvulsant properties in genetically epilepsy-prone rats: prediction of clin. response)  
 RN 150812-13-8 CAPLUS  
 CN Carbamic acid, [2-amino-4-[[[(4-fluorophenyl)methyl]amino]phenyl]-, ethyl ester, dihydrochloride (9CI) (CA INDEX NAME)

L4 ANSWER 11 OF 12 CAPLUS COPYRIGHT 1999 ACS (Continued)



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L4 ANSWER 12 OF 12 CAPLUS COPYRIGHT 1999 ACS  
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AB The title compds., 2-amino-1,4-bis(acylamino)benzene derivs. I (R1 = hydrogen, alkyl, etc.; R3 = alkoxy, amino, etc.; R4, R5 = hydrogen, alkyl;

R6 = arylalkyl) and pharmaceuticals contg. them are claimed. I are anticonvulsants, antipyretics, antiepileptics, muscle relaxants, and peripheral analgesics. Some I were tested as antiepileptics in electroshock-induced convulsions in rats. Reductive carbamoylation of

2-amino-4-[(4-fluorobenzyl)amino]-1-nitrobenzene gave 2-amino-4-[(4-fluorobenzyl)amino]-1-[(ethoxycarbonyl)amino]benzene [ethyl 2-amino-4-[(4-fluorophenyl)methyl]amino]phenyl]carbamate] (II); II dihydrochloride was obtained in 73% yield.

ACCESSION NUMBER: 1993:625705 CAPLUS  
DOCUMENT NUMBER: 119:225705  
TITLE: 1,2,4-triaminobenzene derivatives and a process for

INVENTOR(S): their preparation  
Dieter, Hans Reinhold; Engel, Juergen; Kutscher, Bernhard; Polymeropoulos, Emmanuel; Szelenyi, Stefan;

Nickel, Bernd  
PATENT ASSIGNEE(S): Asta Medica AG, Germany  
SOURCE: Ger. Offen., 11 pp.  
CODEN: GWXBX

DOCUMENT TYPE: Patent  
LANGUAGE: German

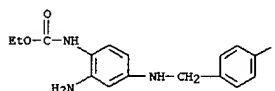
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 4200259	A1	19930715	DE 92-4200259	19920108
EP 554543	A2	19930811	EP 92-121028	19921210
EP 554543	A3	19931027		
EP 554543	B1	19960228		

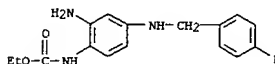
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE

AT 134611	E	19960315	AT 92-121028	19921210
ES 2084914	T3	19960516	ES 92-121028	19921210
CA 2086654	AA	19930709	CA 93-2086654	19930104
ZA 9300011	A	19930805	ZA 93-11	19930104

L4 ANSWER 12 OF 12 CAPLUS COPYRIGHT 1999 ACS (Continued)  
JP 05345752 A2 19931227 JP 93-1054 19930107  
US 5384330 A 19950124 US 93-2458 19930108  
PRIORITY APPLN. INFO.: DE 92-4200259 19920108  
OTHER SOURCE(S): CASREACT 119:225705; MARPAT 119:225705  
IT 150812-12-7P, Ethyl 2-amino-4-[(4-fluorophenyl)methyl]amino]phenyl]carbamate 150812-13-8P, Ethyl 2-amino-4-[(4-fluorophenyl)methyl]amino]phenyl]carbamate dihydrochloride  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of, as antipyretic, analgesic, antiepileptic, anticonvulsant)  
RN 150812-12-7 CAPLUS  
CN Carbamic acid, [2-amino-4-[(4-fluorophenyl)methyl]amino]phenyl]-, ethyl ester (9CI) (CA INDEX NAME)



RN 150812-13-8 CAPLUS  
CN Carbamic acid, [2-amino-4-[(4-fluorophenyl)methyl]amino]phenyl]-, ethyl ester, dihydrochloride (9CI) (CA INDEX NAME)



● 2 HCl

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COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	46.12	166.57
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	-6.43	-6.43

STN INTERNATIONAL LOGOFF AT 11:30:05 ON 24 MAY 1999